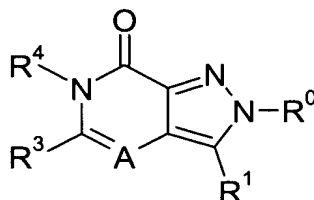


CLAIMS

What is claimed is:

1. A compound of Formula (I)



(I)

wherein

A is N or C(R²), where R² is hydrogen, (C₁-C₄)alkyl, halo-substituted (C₁-C₄)alkyl, or (C₁-C₄)alkoxy;

R⁰ is an optionally substituted aryl or an optionally substituted heteroaryl;

R¹ is an optionally substituted aryl or an optionally substituted heteroaryl;

R³ is hydrogen, (C₁-C₄)alkyl optionally substituted with one or more substituents, or (C₁-C₄)alkoxy; and

R⁴ is a chemical moiety selected from the group consisting of (C₁-C₉)alkyl, aryl, heteroaryl, aryl(C₁-C₅)alkyl, a 3- to 8-membered partially or fully saturated carbocyclic ring(s), heteroaryl(C₁-C₃)alkyl, 5-6 membered lactone, 5- to 6-membered lactam, and a 3- to 8-membered partially or fully saturated heterocycle, where said chemical moiety is optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

2. The compound of Claim 1 wherein A is -C(R²)-; a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

3. The compound of Claim 2 wherein

R² is hydrogen, (C₁-C₄)alkyl, or halo-substituted (C₁-C₄)alkyl;

R³ is hydrogen or (C₁-C₄)alkyl optionally substituted with one or more fluorines; and

R⁴ is a chemical moiety selected from (C₁-C₉)alkyl, aryl(C₁-C₅)alkyl, 3- to 8-membered partially or fully saturated carbocyclic ring, or 3- to 6-membered partially

or fully saturated heterocyclic ring, where the chemical moiety is optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of the compound or the salt.

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4. The compound of Claim 3 wherein

R² is hydrogen;

R³ is hydrogen or methyl;

10 R⁴ is fluoro-substituted (C₁-C₅)alkyl, aryl(C₁-C₅)alkyl, cyclopentyl, cyclohexyl, pyranyl, furanyl, pyrrolidinyl, piperidinyl, or morpholinyl;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of the compound or the salt.

15 5. The compound of Claim 2, 3, or 4 wherein R⁰ and R¹ are each independently a phenyl substituted with 1 to 3 substituents independently selected from the group consisting of halo, (C₁-C₄)alkoxy, (C₁-C₄)alkyl, halo-substituted (C₁-C₄)alkyl, and cyano;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

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6. The compound of Claim 5 wherein R⁰ and R¹ are each independently a phenyl substituted with 1 to 2 substituents independently selected from the group consisting of chloro, fluoro, (C₁-C₄)alkoxy, (C₁-C₄)alkyl, fluoro-substituted (C₁-C₄)alkyl, and cyano;

25 a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

30 7. The compound of Claim 6 wherein R⁰ is 2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl; and R¹ is 4-chlorophenyl, 4-cyanophenyl, 4-trifluoromethylphenyl, or 4-fluorophenyl;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

8. The compound of Claim 7 selected from the group consisting of
6-benzyl-3-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-2,6-dihydropyrazolo[3,4-
c]pyridin-7-one;

6-methyl-3-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-2,6-dihydropyrazolo[3,4-
c]pyridin-7-one;

6-benzyl-2-(2-chlorophenyl)-3-(4-chlorophenyl)-2H-pyrazolo[3,4-c]pyridin-
7(6H)-one;

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-ethyl-2H-pyrazolo[3,4-c]pyridin-
7(6H)-one;

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-isopropyl-2H-pyrazolo[3,4-c]pyridin-
7(6H)-one; and

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-2H-
pyrazolo[3,4-c]pyridin-7(6H)-one;

a pharmaceutically acceptable solvate or hydrate of said compound.

9. The compound of Claim 1 wherein A is nitrogen; a pharmaceutically
acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

10. The compound of Claim 9 wherein

R³ is hydrogen or (C₁-C₄)alkyl optionally substituted with one or more
fluorines; and

R⁴ is a chemical moiety selected from (C₁-C₉)alkyl, aryl(C₁-C₅)alkyl, 3- to 8-
membered partially or fully saturated carbocyclic ring, or 3- to 6-membered partially
or fully saturated heterocyclic ring, where the chemical moiety is optionally
substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of the
compound or the salt.

11. The compound of Claim 10 wherein

R³ is hydrogen or methyl;

R⁴ is fluoro-substituted (C₁-C₅)alkyl, aryl(C₁-C₅)alkyl, cyclopentyl, cyclohexyl,
pyranyl, furanyl, pyrrolidinyl, piperidinyl, or morpholinyl;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of the
compound or the salt.

12. The compound of Claim 9, 10, or 11 wherein R^0 and R^1 are each independently a chemical moiety selected from phenyl or pyridyl, where said chemical moiety is substituted with one or more substituents;

5 a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

13. The compound of Claim 9, 10, or 11 wherein R^0 and R^1 are each independently a phenyl or pyridyl, where said phenyl and said pyridyl are each
10 substituted with 1 to 3 substituents independently selected from the group consisting of halo, (C_1-C_4) alkoxy, (C_1-C_4) alkyl, halo-substituted (C_1-C_4) alkyl, and cyano;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

14. The compound of Claim 13 selected from the group consisting of
2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-3-(6-(trifluoromethyl)pyridin-3-yl)-
2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

3-(5-butylpyridin-2-yl)-2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-2H-
20 pyrazolo[4,3-d]pyrimidin-7(6H)-one;

3-(4-chlorophenyl)-2-(3,5-dichloropyridin-2-yl)-6-(2,2,2-trifluoroethyl)-2H-
pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-3-(6-chloropyridazin-3-yl)-6-(2,2,2-trifluoroethyl)-2H-
pyrazolo[4,3-d]pyrimidin-7(6H)-one;

25 2-(2-chlorophenyl)-3-(6-chloropyridin-3-yl)-6-(2,2-difluoropropyl)-2H-
pyrazolo[4,3-d]pyrimidin-7(6H)-one; and

3-(4-chlorophenyl)-2-(3-chloropyridin-2-yl)-6-(2,2,2-trifluoroethyl)-2H-
pyrazolo[4,3-d]pyrimidin-7(6H)-one;

a pharmaceutically acceptable solvate or hydrate of said compound.

15. The compound of Claim 13 wherein R^0 and R^1 are each independently a phenyl substituted with 1 to 2 substituents independently selected from the group consisting of chloro, fluoro, (C_1-C_4) alkoxy, (C_1-C_4) alkyl, fluoro-substituted (C_1-C_4) alkyl, and cyano;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

16. The compound of Claim 15 wherein R⁰ is 2-chlorophenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2-chloro-4-fluorophenyl, or 2,4-difluorophenyl; and R¹ is 4-chlorophenyl, 4-cyanophenyl, 4-trifluoromethylphenyl, or 4-fluorophenyl;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

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17. The compound of Claim 16 selected from the group consisting of 3-(4-chlorophenyl)-2-(2-ethylphenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-3-(4-propoxyphenyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

3-(4-butylphenyl)-2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-6-(2,2-difluoropropyl)-3-(4-methoxyphenyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

3-(4-bromophenyl)-2-(2-chlorophenyl)-6-(2,2-difluoropropyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-3-(4-chlorophenyl)-5-ethyl-6-(2,2,2-trifluoroethyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-bromophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-6,7-dihydro-5-methyl-7-oxopyrazolo[4,3-d]pyrimidin-2-yl)benzonitrile;

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2-difluoropropyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

3-(4-bromophenyl)-2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-3-(4-ethylphenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

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2-(3-(4-chlorophenyl)-6-(2,2-difluoropropyl)-6,7-dihydro-5-methyl-7-oxopyrazolo[4,3-d]pyrimidin-2-yl)benzonitrile;

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

5 2-(2-bromophenyl)-3-(4-chlorophenyl)-6-(2,2-difluoropropyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-3-(4-(trifluoromethyl)phenyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

10 2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2-difluoropropyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one; and

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

a pharmaceutically acceptable solvate or hydrate of said compound.

15 18. The compound of Claim 17 selected from the group consisting of 2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-bromophenyl)-3-(4-chlorophenyl)-6-(2,2-difluoropropyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

20 2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-3-(4-(trifluoromethyl)phenyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2-difluoropropyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one; and

25 2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

a pharmaceutically acceptable solvate or hydrate of said compound.

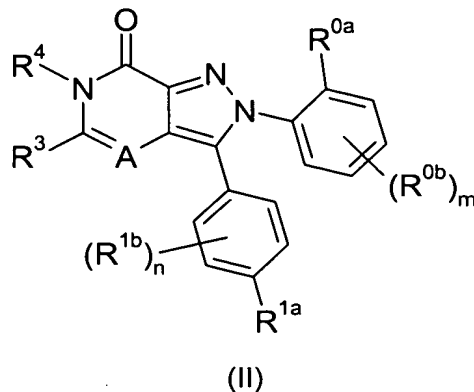
19. The compound of Claim 18 which is 2-(2-chlorophenyl)-3-(4-chlorophenyl)-6-(2,2,2-trifluoroethyl)-5-methyl-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

30 a pharmaceutically acceptable solvate or hydrate of said compound.

20. The compound of Claim 18 which is 2-(2-chlorophenyl)-6-(2,2,2-trifluoroethyl)-3-(4-(trifluoromethyl)phenyl)-2H-pyrazolo[4,3-d]pyrimidin-7(6H)-one;

a pharmaceutically acceptable solvate or hydrate of said compound.

21. A compound of Formula (II)



wherein

A is N or C(R²), where R² is hydrogen, (C₁-C₄)alkyl, halo-substituted (C₁-C₄)alkyl, or (C₁-C₄)alkoxy;

R^{0a}, R^{0b}, R^{1a}, and R^{1b} are each independently halo, (C₁-C₄)alkoxy, (C₁-C₄)alkyl, halo-substituted (C₁-C₄)alkyl, or cyano;

n and m are each independently 0, 1 or 2;

R³ is hydrogen, (C₁-C₄)alkyl optionally substituted with one or more substituents, or (C₁-C₄)alkoxy; and

R⁴ is a chemical moiety selected from the group consisting of (C₁-C₉)alkyl, aryl, heteroaryl, aryl(C₁-C₅)alkyl, a 3- to 8-membered partially or fully saturated carbocyclic ring(s), heteroaryl(C₁-C₃)alkyl, 5-6 membered lactone, 5- to 6-membered lactam, and a 3- to 8-membered partially or fully saturated heterocycle, where said chemical moiety is optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

22. The compound of Claim 21 wherein

A is -C(R²)-;

R² is hydrogen, (C₁-C₄)alkyl, or halo-substituted (C₁-C₄)alkyl;

R³ is hydrogen or (C₁-C₄)alkyl optionally substituted with one or more fluorines; and

R⁴ is a chemical moiety selected from (C₁-C₉)alkyl, aryl(C₁-C₅)alkyl, 3- to 8-membered partially or fully saturated carbocyclic ring, or 3- to 6-membered partially or fully saturated heterocyclic ring, where the chemical moiety is optionally substituted with one or more substituents;

5 a pharmaceutically acceptable salt thereof, or a solvate or hydrate of the compound or the salt.

23. The compound of Claim 22 wherein

R² is hydrogen;

10 R³ is hydrogen or methyl;

R⁴ is fluoro-substituted (C₁-C₅)alkyl, aryl(C₁-C₅)alkyl, cyclopentyl, cyclohexyl, pyran-
yl, furanyl, pyrrolidinyl, piperidinyl, or morpholinyl;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

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24. The compound of Claim 21 wherein

A is nitrogen;

R³ is hydrogen or (C₁-C₄)alkyl optionally substituted with one or more fluorines; and

20 R⁴ is a chemical moiety selected from (C₁-C₉)alkyl, aryl(C₁-C₅)alkyl, 3- to 8-membered partially or fully saturated carbocyclic ring, or 3- to 6-membered partially or fully saturated heterocyclic ring, where the chemical moiety is optionally substituted with one or more substituents;

25 a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

25. The compound of Claim 24 wherein

R³ is hydrogen or methyl;

30 R⁴ is fluoro-substituted (C₁-C₅)alkyl, aryl(C₁-C₅)alkyl, cyclopentyl, cyclohexyl, pyran-
yl, furanyl, pyrrolidinyl, piperidinyl, or morpholinyl;

a pharmaceutically acceptable salt thereof, or a solvate or hydrate of the compound or the salt.

26. A pharmaceutical composition comprising (1) a compound of Claim 1, or a solvate or hydrate of said compound; and (2) a pharmaceutically acceptable excipient, diluent, or carrier.

5 27. The composition of Claim 26 further comprising at least one additional pharmaceutical agent.

28. The composition of Claim 27 wherein said additional pharmaceutical agent is a nicotine receptor partial agonist, an opioid antagonist, a dopaminergic agent, an attention deficit disorder agent, or an anti-obesity agent.

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29. The composition of Claim 28 wherein said anti-obesity agent is selected from the group consisting of an apo-B/MTP inhibitor, a 11 β -hydroxy steroid dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR-4 agonist, a CCK-A agonist, a monoamine reuptake inhibitor, a sympathomimetic agent, a β_3 adrenergic receptor agonist, a dopamine agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT_{2c} receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a ciliary neurotrophic factor, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

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30. A method for treating a disease, condition or disorder which is modulated by a cannabinoid receptor antagonist in animals comprising the step of administering to an animal in need of such treatment a therapeutically effective amount of a compound of Claim 1;

30 a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.

31. The method of Claim 30 wherein said compound is administered in combination with a nicotine receptor partial agonist, an opioid antagonist, a dopaminergic agent, an attention deficit disorder agent, or an anti-obesity agent.

5 32. The method of Claim 31 wherein said anti-obesity agent is selected from the group consisting of an apo-B/MTP inhibitor, a 11β -hydroxy steroid dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR-4 agonist, a CCK-A agonist, a monoamine reuptake inhibitor, a sympathomimetic agent, a β_3 adrenergic receptor agonist, a dopamine agonist, a melanocyte-stimulating
10 hormone receptor analog, a 5-HT_{2c} receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like
15 peptide-1 receptor agonist, a ciliary neurotrophic factor, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

20 33. The method of Claim 30 wherein said disease, condition or disorder modulated by a cannabinoid receptor antagonist is selected from the group consisting of weight loss, obesity, bulimia, depression, atypical depression, bipolar disorders, psychoses, schizophrenia, behavioral addictions, suppression of reward-related behaviors, alcoholism, tobacco abuse, dementia, seizure disorders, epilepsy, attention deficit disorder, Parkinson's disease, inflammation,
25 gastrointestinal disorders, and type II diabetes.

34. The method of Claim 33 wherein said disease, condition or disorder modulated by a cannabinoid receptor antagonist is obesity, bulimia, attention deficit disorder, Parkinson's disease, dementia, alcoholism, or tobacco abuse.

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35. A method for treating a disease, condition or disorder modulated by a cannabinoid receptor antagonist comprising the step of administering a pharmaceutical composition of Claim 26.

36. The method of Claim 35 wherein said pharmaceutical composition further comprises an additional pharmaceutical agent.

37. The method of Claim 36 wherein said additional pharmaceutical
5 agent is a nicotine partial agonist, an opioid antagonist, a dopaminergic agent, an attention deficit disorder agent, or an anti-obesity agent.

38. The method of Claim 37 wherein said anti-obesity agent is selected from the group consisting of an apo-B/MTP inhibitor, a 11 β -hydroxy steroid
10 dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR-4 agonist, a CCK-A agonist, a monoamine reuptake inhibitor, a sympathomimetic agent, a β_3 adrenergic receptor agonist, a dopamine agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT_{2c} receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin
15 antagonist, a lipase inhibitor, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a ciliary neurotrophic factor, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist
20 or inverse agonist, and a neuromedin U receptor agonist.

39. The method of Claim 35, 36, 37 or 38 wherein said disease, condition or disorder modulated by a cannabinoid receptor antagonist is obesity, bulimia, attention deficit disorder, Parkinson's disease, dementia, alcoholism, or
25 tobacco abuse.

40. A method for treating a disease, condition or disorder modulated by a cannabinoid receptor antagonist in animals comprising the step of administering to an animal in need of such treatment two separate pharmaceutical compositions
30 comprising

- (i) a first composition comprising a compound of Claim 1 or 21, and a pharmaceutically acceptable excipient, diluent, or carrier, and

- (ii) a second composition comprising at least one additional pharmaceutical agent and a pharmaceutically acceptable excipient, diluent, or carrier.

5 41. The method of Claim 40 wherein said at least one additional pharmaceutical agent is a nicotine partial agonist, an opioid antagonist, a dopaminergic agent, an attention deficit disorder agent, or an anti-obesity agent.

10 42. The method of Claim 41 wherein said anti-obesity agent is selected from the group consisting of an apo-B/MTP inhibitor, a 11 β -hydroxy steroid dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR-4 agonist, a CCK-A agonist, a monoamine reuptake inhibitor, a sympathomimetic agent, a β_3 adrenergic receptor agonist, a dopamine agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT_{2c} receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a ciliary neurotrophic factor, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

25 43. The method of Claim 40 wherein said first composition and said second composition are administered simultaneously.

 44. The method of Claim 40 wherein said first composition and said second composition are administered sequentially and in any order.

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